MEETING

SCIENTIFIC REVIEW PANEL

ON TOXIC AIR CONTAMINANTS

PENINSULA ROOM I

RADISSON INN

275 SOUTH AIRPORT BOULEVARD

SOUTH SAN FRANCISCO, CALIFORNIA

THURSDAY, MAY 21, 1992

9:50 A.M.

Nadine J. Parks
Shorthand Reporter

PETERS SHORTHAND REPORTING CORPORATION

3336 BRADSHAW ROAD, SUITE 240
SACRAMENTO, CALIFORNIA 95827
TELEPHONE (916) 362-2345

MEMBERS PRESENT

Dr. James Pitts, Chair

Dr. Charles Becker

Dr. Thomas Davis

Dr. Gary Friedman

Dr. James N. Sieber

Dr. Hanspeter Witschi

Staff:

From the Air Resources Board:

Bill Lockett
Genevieve Shiroma
Bruce Oulrey

From the OEHHA:

Dr. George Alexeeff
Dr. Lauren Zeise

From the Department of Pestice Regulation:

Dr. James Wells, Director

I N D E X

INDEX, continued. . .

P R O C E E D I N G S

--o0o--

CHAIRMAN PITTS: Good morning. I apologize for the delay in getting things started, but as we said, it's one of those California phenomena of terrible tieups on the freeway. So, I appreciate your patience. Since you've been in similar experiences yourselves, you can understand where we're coming from.

All right. The first item on the agenda for today's meeting is a discussion of the best value of risk for perc as set forth in the Office of Environmental Health Hazard Assessment's April 13th, 1992 document, "Revisions to the Technical Support Document, Part B, Proposed Identification of Perchloroethylene as a Toxic Air Contaminant."

The discussion will be led by Dr. George Alexeeff and your colleague next to you.

DR. ALEXEEFF: I'm George Alexeeff, and with me is Dr. Lauren Zeise, and she is the Section Chief of our Risk Assessment Group for Prop 65.

CHAIRMAN PITTS: We appreciate your being here for this, too, Lauren.

DR. ALEXEEFF: The Office of Environmental Health Hazard Assessment, OEHHA, is submitting changes to the Scientific Review Panel to lower OEHHA's best cancer

potency value from 54 times 10 to the minus 6 per part per billion to 40 times 10 to the minus 6 per part per billion. This is a 26 percent reduction of the estimated cancer potency of perchloroethylene.

The basis for this reduction is OEHHA's decision to lower estimates of human metabolism of perchloroethylene at ambient levels from 25 to 18.5 percent.

We're proposing to do this as a result of new model calculations conducted by Dr. Dale Hattis of Clark University, which was presented at the February 4th workshop on perchloroethylene.

As you will recall, our risk assessment for perchlorethylene is based on a pharmacokinetic model of exposure. There are several pharmacokinetic models for perchloroethylene, and we have chosen the one developed by Dr. Hattis as our best value.

So, as the model calculations are updated, it's reasonable to update the risk assessment. The range of human risks remains unchanged; that is, 2 to 72 times 10 to the minus 6 per part per billion.

The information that we presented -- that I'll be presenting was presented to the Scientific Review Panel on March 19th, 1992, when the Panel asked that we essentially put it in writing and submit it for public comment. So, the proposed change of the best value has been

submitted for public comment on April 13th, 1992, and we received several comments regarding the proposed change.

Just to comment on the change. By changing the best value required changing a number of tables and just pages, just bringing them all up to date and consistency.

The first comment I'd like to mention is dated May 13th, 1992, from B. J. Kirwan of Latham and Watkins. And it states that -- and I made copies of them. And I'm just going to read the comments and responses. And there are copies for the audience on the table out in back, and I think the Panel members have copies.

At the February 4th workshop, Dr. Richard Rietz presented data supporting a metabolism level of two to three percent.

And our response is that at the workshop, Dr. Reitz presented data which supports his pharmacokinetic model and his coice of model parameters. And this information is presented in OEHHA's health assessment document on perchloroethlene.

Two to three percent represents lower values in the range of human metabolism. New in vitro data developed in December and January were presented at the workshop as well. As discussed at the workshop, the studies appear to have been done at saturating conditions.

At the concentration tested, the -- and this was discussed to a fairly large extent. And, in fact, Dr. Rietz indicated that he had to do it in saturating concentrations because of the limited detection of the system he was using.

At the concentration tested, the in vitro study estimate of human metabolism is consistent with both the Hattis/Ikeda and the Reitz models in terms of whole body metabolism. That is, when we took the in vitro data and ran it through the two pharmacokinetic models -- Dr. Rietz' model and the Hattis model -- they were both consistent because of the saturating concentrations that were used in the in vitro study.

However, for the rodents, the in vitro study rates were not consistent with predictions from either the Hattis or Ikeda -- Hattis/Ikeda or the Rietz models. Thus, OEHHA believes that the preliminary data provide qualitative information, but cannot be used quantitatively.

Cammer and Associates have sent a comment, and --

CHAIRMAN PITTS: Would you want to have the Panel consider their reactions to these comments on a step-by-step basis?

DR. ALEXEEFF: That's fine.

CHAIRMAN PITTS: Well, let's do that. Or would you like to hear all of them first?

DR. ALEXEEFF: There are four comments and they're all sort of interrelated.

CHAIRMAN PITTS: Okay. That's fine.

DR. ALEXEEFF: Okay. I'll speak up a little bit.

Cammer and Associates sent some comments. One was dated May 19th, 1992, and similar comments were sent by B. J. Kirwan of Latham and Watkins in a letter dated May 13th, and also on February 27th.

And the comment is that the 18.5 percent metabolism figure was chosen from an inappropriate data set. And the dermal exposure occurred in those workers. Virtually all other data show two to three percent metabolism of perchloroethylene. And the in vitro studies performed in December and January confirm the two to three percent metabolism.

Our response is, as discussed in the OEHHA health risk assessment document, there's a wide range of metabolism estimates for perchloroethylene in humans, approximately two to 50 percent of the inhaled dose.

The physiological upper limit reported by Bogen and McKone in '88 is 73 percent. And they also estimate a range of metabolism between 5 and 65 percent of the physiological limit; that is, approximately 4 to 47 percent.

Dr. Hattis presented at the workshop that the range of metabolism reported using various pharmacokinetic models is .7 to 55 percent. Now, this variation is in part due to the higher metabolism estimated at environmental levels compared to those in the available human studies.

The available human data are consistent with greater metabolism at lower concentration levels. At higher concentrations, perchloroethylene metabolism is saturated and a lower percentage is metabolized.

OEHHA choise the 18.5 percent as the estimate for human metabolism based on the Ikeda study and Dr. Hattis' pharmacokinetic model. The Ikeda study is a fairly large study, about 34 workers, and encompasses a fairly broad range of exposure. And up to five air samples were taken at each work station. The study indicates that the workers supervised an automated process and no mention is made of dermal exposure or contact dermatitis.

So, there were comments saying that this study -- there was dermal contact, but in the original study there's no mention of even a chance of dermal contact occurring in these workers. So, there's no real documentation that there is any dermal contact.

The Ikeda value is not inconsistent with the other

values when they're projected to environmental doses.

Various studies have shown that perc metabolism varies with such factors as age, sex, exercise rate, body mass, and adipose tissue level. Even Dr. Rietz' recent in vitro study shows a fourfold variation in metabolism in human liver tissue.

The Ikeda study has also been used in published analyses by Dr. Curtis Travis in his risk assessment of perchloroethylene and by Dr. Keneeth Bogen in his group's risk assessment of perchloroethylene.

Consequently, other leading researchers have found the Ikeda study useful in characterizing the risks of perchloroethylene. OEHHA staff believes that the choice of 18.5 percent metabolism incorporates much of the variation among humans.

I'm going to skip the next comment and take it up at the end. It's more procedural.

The next comment was made by Cammer and Associates, and that is that an upperbound estimate of human metabolism should not be used in risk assessment.

And our response is that the OEHHA risk assessment presents a range of upperbound unit risks for perchloroethylene from 2 to 72 times 10 to the minus 6 per part per billion.

The ARB asked OEHHA to choose a value from that

range for the best upperbound value on cancer risk.

The purpose of the best value is to provide a reasonable upper estimate for unit risk. The 18.5 percent does not reflect an actual upperbound estimate of metabolism in humans. Instead, the 18.5 percent metabolism rate reflects a best estimate of metabolism from the Ikeda study. And the value calculated from the study has been reerred to as a plausible upper limit for metabolism.

So, that is -- in other words, people have characterized the Ikeda study as an upper limit in terms of the number is higher than the other studies at the occupational exposure levels.

The range of human metabolism reported in the OEHHA document on perc -- as I already mentioned -- is 2 to 50 percent. Thus, an upper limit would be actually closer to 50 percent.

OEHHA staff believe that the metabolism rate used should reflect the variation of metabolism in the neterogeneous human population. Available data indicate that metabolism of perc is highly variable. Some factors which influence metabolism are the exposure concentration, the age, sex, exercise rate, body mass, and adipose tissue level. Use of a 2 or 5 percent estimate of metabolism would not result, in our opinion, in the best upperbound value for risk, because it would not be protective of many

individuals. The 2 to 5 percent values reflect metabolism at high exposure levels where saturation of metabolism occurs.

So, one of the difficulties in determining what is the metabolism rate at environmental levels is that most of the studies were done at occupational levels, which is above the saturation rate for perchloroethylene metabolism.

So, you have to do some back calculations and make some estimations.

I'd just like to mention that there are -- there are other uncertainties in the risk assessment that are documented, and one is that there is considerable variability in other pharmacokinetic input parameters that are not taken into account in the risk assessment. And another is that the metabolic pathway leading to the active carcinogenic metabolite has not been identified. And the risk assessment focuses on calculating the dose based on only one of the metabolic pathways, and you have the glutathion pathway and its relationship to -- potential relationship to carcinogenicity.

And I'll just go back to that last comment. A comment was made by both Latham and Watkins and Cammer and Associates that the basic differences among the scientists should be discussed at a meeting of the Scientific Review

Panel. And it's our opinion at OEHHA that this is a decision to be made by the Scientific Review Panel and not OEHHA's decision.

We also received some additional comments from -- some letters from AC Products, Incorporated, and Crystal Cleaners. However, they were not specifically related to the best value change. And yesterday, I also received a copy of a letter sent to Secretary Strock of Cal-EPA from Paul Cammer, and that letter deals primarily with his concerns about the process, particularly the SRP's involvement in the process. So, I won't particularly comment on that either.

That closes my comments.

CHAIRMAN PITTS: Thank you very much, George. We're open for discussion. Chuck, you were at that meeting. Perhaps you can lead off. You were at the workshop.

DR. BECKER: Yes. I guess I was surprised that there was some idea that our committee was not given the information. In fact, two of us attended the meeting, and we had open discussion about what the information was. The scientific uncertainties were addressed. The question of saturation was openly discussed. And it was very clear that there were some uncertainties. So, I was surprised that they would consider that we hadn't been informed about this at all. I was surprised. In fact, I don't think that's

been the case. In fact, I think it's been the opposite. Dr. Froines was on the panel and was there and discussed that. So, I think that the process has been handled extremely well.

So, my response would be that the process has been about as open and scientific as is possible. Others may feel differently.

CHAIRMAN PITTS: Yes?

DR. SIEBER: Jim, it would be helpful to me if George would walk is through in fairly simple terms the connection between human metabolism rate and the unit risk factor that we're ultimately going to want to come up with.

CHAIRMAN PITTS: Why don't we do that, and then we'll come back to the process. We also have a letter now. A Fax just came in from John Froines. So, let's do this.

DR. ALEXEEFF: Our stand approach for risk assessment would be to take the regular concentration used in an animal study, and we take that concentration and adjust it to an average daily rate, and then put it in our risk assessment model, linearized multistage model, and calculate the cancer potency.

And in this -- for perchloroethylene, that is what we would -- suggested originally when we sent out the

document. And the comments came back saying that we should use a pharmacokinetic model for the risk assessment.

Now, what a pharmacokinetic model does is -- sort of two major attributes of it. First of all, we can -- I'm sure you're all aware what the model is.

The model essentially describes the absorption, metabolism, elimination, and maybe target tissue dose and target tissue concentration of the chemical.

So, you can do that calculation for the animal study itself. So, in other words, if you assume that the levels were high in the animal study and maybe some saturation occurred, and metabolites poured over into a pathway, you can correct for that using this physiologic model. And there are a lot of -- it depends on the model, but may be 40 equations and a number of parameters have to be taken from the literature estimated for this model.

So, you can do it with just the animal data. Then, you can also -- and we did that for methylene chloride.

Now, the next step is, you can say that it's not simply the question of what happened in the animal experiment that needs to be corrected, but there are differences in the metabolism processing of humans versus animals or the animal in question.

And, therefore, you can take that data and build

a pharmacokinetic model for the humans. And that is what--essentially the first model was developed by Dr. Rietz of Dow for this chemical. And he built the pharmacokinetic model, and then showed that humans metabolize perchloroethylene differently than animals do.

Since then, there have been a number of other models -- about five other models have come out. And so, you take all the human data and put it in, and then it adjusts the potency, the amount of actual metabolite that reaches the target tissue, which in this case is the liver.

Now, the way the metabolism works out is that a lot of the input parameters -- although I said there's a lot of equations and a lot of information that gets put in, sometimes they may not affect the final result that much.

One of the key parameters in this case happens to be metabolism, and what is the relative metabolism between humans versus mice. Because perchloroethylene is thought that it's the metabolite that causes cancer, not the parent compound.

So, if mice metabolize more perchloroethylene than humans, they're going to get more of the cancer causing agent in the body than a human does.

So, that is what we assumed. The debate is simply how much more do mice metabolize perchloroethylene than

DR. SIEBER: George, the active metabolite is the oxide on your --

DR. ALEXEEFF: Right. Well, it hasn't been identified, but it's assumed by that pathway that that is -- it's not clear if it's the oxide in terms of that. There's also TCA at one point was considered to be the major active metabolite. So, there's been discussion about the end product TCA. In the document, there's a couple of metabolites that have been identified to be genotoxic. There's no consensus on what is the active metabolite. But it's assumed to be somewhere down that pathway.

DR. SIEBER: I think what I'm getting at is, I can buy -- see the argument about the metabolism rates. Now, the question is, at the greater metabolism rate, do you also generate more of the active metabolite. Has that connection been made?

DR. ALEXEEFF: That's a good question. That's one of the uncertainties. And the next step is activation versus detoxification and the relative rates of those.

So, there's more questions to be answered in general on this, but this is certainly a more sophisticated-- I think generally everybody agrees it's a more accurate estimate of the concentration than just the outdoor concentration or the ambient concentration.

CHAIRMAN PITTS: Let's go around the table.

DR. FRIEDMAN: I have nothing to add.

DR. BECKER: I'd just add that we used that in methylene chloride before you came, and I think that everyone agreed that that allowed us go to the next level of understanding the sophistication.

However, we still don't know what causes cancer, and we're not sure which metabolite it is. So there's still those uncertainties. But then the question is, is this process -- are those uncertainties covered.

And one argument is, well, the metabolism -- if it were two to three percent would be different than if it was 17 percent -- I think the number they've chosen is 18 percent. So, that certainly incorporates that range. The question is, which range do you use, and does it change from 25 to 18, and is that appropriate in light of this new information?

The second thing is, given that amount of information, does that really -- is that really going to change anything? And I think, the best I can understand it, it's certainly clear that that's within a reasonable range of what you would expect with all the uncertainties.

CHAIRMAN PITTS: Tom?

DR. DAVIS: I can't comment on the technical aspects of the model. I just have to assume that the

people whose expertise is in that area, that they have concluded, as others have been trying to get it clear to them. I'm fairly satisfied that 25 and 18 are different, but to what extent? I'm satisfied that 18 is the real number as opposed to two to three. It's difficult.

CHAIRMAN PITTS: Dr. Witschi?

DR. WITSCHI: Yes. Please excuse me. Refresh my memory. Where did the 24 percent come from in the original one?

DR. ALEXEEFF: There was -- in Dr. Hattis' original model, which was released I guess in '87, that's when he had the 24 percent. And since then, he's updated -- he's added additional components on his model, and now he's differentiated between oral and inhalation exposure. So, the 25 -- 24.9, or whatever it was, comes from his original documentation of the model.

DR. WITSCHI: Okay.Now, the 18.5 percent out of the Ikeda study, is this in the study itself?

What was the conclusion of the guy who did the work?

DR. ALEXEEFF: Well, the general purpose of the work was not what we're using it for. They were trying to see if TCA in the urine is a good predictor of exposure to perchloroethylene in the workplace. They were trying to find a monitoring, you know, biomarker. And that's

generally been the interest of almost all the human metabolism studies. I can't say for sure, but I think it's probably all of them that are looking for markers primarily.

So, they don't generally generate the metabolism rate. They give information on -- well, first of all, the biggest problem is there's no mass balance for the chemical. It's not a radio labeled chemical. So, there's simply estimates on what the breathing rate was, you know, how much was absorbed, and things like that.

And then the studies have looked at levels of primarily trichloro compounds in the urine, because that can be measured.

DR. WITSCHI: Well, not knowing exactly how much went in --

DR. ALEXEEFF: Right. They don't know exactly how much went in, and we have a concern that measuring trichloro compounds is not measuring exactly how much is coming out either.

The measurements generally -- I don't recall any of the studies going more than a half life, a single half life, roughly half life up to less than a half life.

So, the conclusions of the studies were primarily what focused on whether or not it is or is not a good surrogate for perc exposure. They weren't generally

commenting on what the metabolism rate of perchloroethylene is. Instead, people can take that data that was presented in these papers and put them into these pharmacokinetic models. For each of those studies, you have to do that.

And when you do that, the paper presents, as I say, most of the information. You have to come up with some of the other estimates as well, such as what was the breathing rate, and things like that.

DR. ZEISE: It might be useful to point out that when we examined all four different major sources of human in vitro data, we found that at low doses they weren't all consistent. There was a lot of uncertainty for each study. And they were all consistent with this value 18 percent at low doses.

The problem is there is saturation at high doses. And so, the metabolism that you would calculate at high doses is very different from the low doses. But we do have consistency across the four data sets.

DR. SIEBER: I like the explanation. I think the staff has done a very careful job in trying to select the best number. They've had to sort through a lot of uncertainty and come up with their best estimate, which I tend to agree with.

Could we maybe go over to addressing the concerns of the industry? Obviously, there's much concern. We

received an unusual number of letters at the last minute.

George, maybe you could explain the ramifications for the individual operator in adopting one number over the other. Is this right at the critical line where people will actually be unable to operate in your opinion?

DR. ALEXEEFF: Well, this probably is a better -- something the ARB staff should address, as to what the impact is, since we just assess the risk, and they implement --

DR. SIEBER: And I don't want to scare them away if you've got more questions.

DR. ALEXEEFF: I'll stay here.

CHAIRMAN PITTS: Ms. Shiroma.

MS. SHIROMA: Yes.

CHAIRMAN PITTS: It's a good question.

MS. SHIROMA: Right. Yes, Dr. Sieber, in response to --

CHAIRMAN PITTS: Genevieve, we can't --

MS. SHIROMA: Sorry, Nadine.

Well, first of all, to set the stage, I think the Panel realizes what your charge is here, as far as looking at the science and assuring that you're making a decision based on that full set of information.

Now, once we step into the arena of risk management, there has been a lot of discussion about the

implications of the information that comes out of this process. And one of the major things that was brought up through the Board hearing process and through our discussions with the industry is that the air pollution control districts of California have their own permitting programs for permitting new dry cleaners or other kinds of industrial sources.

And a number of the districts now have permitting programs for sources of toxic pollutants. The concern is that the way the districts are making their decisions is that they are using the best value to calculate an estimated risk in determining whether or not a source then receives a permit.

They're also using this information for notifying the public as to whether or not there may be a health risk. So, yes, this information would then go on, be provided to our Board, and then provided to the districts to incorporate in their programs.

Now, the Board recognized last October that there is this implication. They also recognized the uncertainties that go into coming up with these best values. So, they have instructed the staff to work with the districts, affected industry, the public, yourselves to look at the risk management process and determine if the current process is working or whether some changes may

be necessary.

So, we are now embarking upon that. We've held a number of workshops. As far as current permitting goes, many districts are holding off on making decisions about incorporating new numbers for the best values for particular pollutants into their programs.

The Bay Area District is in the midst of their program in terms of permitting and the implications, and they're working right along with us to look at this issue.

So, granted, yes, there's implications from what you do. We recognize it in the risk management arena, and we're trying to work on this very expeditiously.

So, does that help?

DR. FRIEDMAN: Could you put it in sort of simple terms? Is the average dry cleaner going to have to shut down because of the new standards?

MS. SHIROMA: No. No. The average dry cleaner is not going to have to shut down. That's our view. I know there are differing opinions, and there are many people in the industry who are very concerned about this.

Our view is that we are looking at developing a control measure for existing dry cleaners. We're holding workshops on that as part of our toxics program. The intent there is not to shut anybody down. The intent is to do what's fair and equitable.

As far as looking at new dry cleaners or modifying facilities, that's where some of these questions come in as to whether or not there will be an easy way for new dry cleaners to site. And that is really the arena that we're working on at this point.

And there has been some question about that. The districts are very aware of this. Their intention is not to stop new facilities from coming in. They are simply trying to implement their permitting programs in a fair and equitable manner. As I say, we recognize the situation, and we're working with them through this summer on this.

DR. ALEXEEFF: The current number we're operating on is an EPA number that has never been officially approved. It was released in draft in 1986. The EPA has never been able to finalize its process.

CHAIRMAN PITTS: Is that about 6 or something?

DR. ALEXEEFF: Yes, 6.5. And that number has never been allowed to go to completion. So, there will be more facilities that would meet whatever -- you have a cut-off of some sort that would need some sort of notification requirement.

Right now, the number of facilities at the current number -- the current risk number, the old EPA number, already meet, you know, whatever kind of line you

might draw, which is usually one in a hundred thousand risk. A number of facilities are already over that. This obviously would make more facilities over that number, too.

I think that one area that -- what could happen is that, you know, the estimates of the risk in the facilities are based upon estimates of ambient concentrations and not monitored data in general. So, there's a lot of information to be gained in that arena. Generally, they just have been looking at the amount of perchloroethylene used and assuming it's all -- all goes up the stack and is all distributed evenly. And we, of course, know a lot of it goes other places -- on the clothes and things like that.

So, I think that there is a lot more information that needs to be gathered. This will probably force that gathering of information.

MS. SHIROMA: Just to be sure I answered your question. Your question was, are existing dry cleaners going to be shut down as a result of your action today; the answer is, no. That will not occur.

CHAIRMAN PITTS: Basically, for example, under the findings -- we have the original findings, but basically they're the same form. We'll discuss and vote on the number in a moment. But the findings five a range. And

this has not changed. You have not changed the range.

That's important, the range. And either I have -- there has been a flaw in the Xerox copy, or it's .2 or is it 2?

DR. ALEXEEFF: It's 2.

CHAIRMAN PITTS: It's 2. Okay. I see a .2 here. It's not a floater. I watch those go by, too, occasionally. The range of risk is given in here. This is an important point, because there's been some implications that you've raised, and some communication to Jim Strock that the Panel has not looked at the entire information.

It clearly says here that it's 2 to 72. And then we say that the value that -- either the 70 or the 50 -- or the 40 now, it says the range remains unchanged. This estimate of the value represents the upper range of plausible excess cancer risk. The actual risk may be significantly lower.

And I think, throughout, as we agree on the Panel, we agree that very carefully those words have been put in here and to state that this is basically the ball park. It's protective of health, by there's a wide range. That's point one.

Point 2, as I understand it -- this is then the scientific evaluation of the SRP. This is science. This is the science part of the entire operation. When this goes

to the ARB, they examine this.

And I gather where the problems arise is, in a sense -- you said that the bright blue lines that the -- districts have certain numbers, and when those numbers come up, flash up, then certain actions have to be taken. Those numbers don't necessarily recognize the fact that the range is 2 to 72. They have an option, if they wish -- either have an option or can develop an option through changing their regulations to accept a different number than the number that's represented in our findings.

And that's a matter of discussion between actually the districts and OEHHA, and it's not in the province of SRP. Is that basically correct the way I phrased it?

MS. SHIROMA: Yes. I think you've given a good general depiction. In the risk management, we have some other options of criteria that can be considered in making those kinds of decisions.

DR. WITSCHI: I have a question on this range, George. I'm glad you're talking about the range. Was this range based on 18.5 metabolism, or would it include people, metabolism 2 percent, and people with --

DR. ALEXEEFF: The lower numbers are the two to three percent.

DR. WITSCHI: That should be made clear probably.

CHAIRMAN PITTS: That's a good idea. It might be made clear in the findings, too.

Make a note of that. Genevieve, you want to do that? Put that in the findings.

That's a very good point.

MS. SHIROMA: Are you ready to discuss the findings?

CHAIRMAN PITTS: Before we do, I'd like to to bring in one other important set of comments from Dr. Froines. Dr. Froines, as Dr. Becker pointed out, was also at the workshop. And actually, he was the leadperson on Part B on perc. And he, unfortunately, due to a major commitment that came up, was unable to attend personally here. But he has read the material and has Faxed to us a two-page letter that gives in detail his comments on the proposed changes. And I'd like these to go into the minutes or the record. And I wondered, Chuck, since you were there with him, I think reading his comments -- if we could take the time to read them for the audience and for the record, or do you think that might be sensitive?

DR. BECKER: I think they've already been summarized in part by George, and that is that there was no question that all of us who attended and addressed this science were aware of the scientific issues that

surrounded this compound. We've discussed them here today, and the major problem is, as George explained, that no mass balance study had really been done to give us all the parameters necessary for all these equations.

So, the end result of all that uncertainty we've addressed. And we've also seen, that even though there's difference in the metabolism, 25 to 18 or 2 to 3, that the ultimate number doesn't change in this assessment.

So, my reading of John's -- and I also discussed this with him when we were there -- was that our charge was to take the most health conservative approach, and that's what's been done. And so, his conclusion is that this document is not seriously flawed; that it incorporates all the parameters that we would normally deal with in this setting. And he recommends that we accept this as good science.

I think he also -- I don't know whether this is the time to discuss it or not, but I also share with Dr. Froines his opinion in the last paragraph that we were provided some distorted view of this -- and I don't think that's correct at all. In fact, I think we were the ones who pushed to see that this was clearly brought out in the open and discussed. And the issues concerning this add more, I think, to the fact that this is an open process and has been fully discussed. And I think we're clear, as a Panel,

over exactly how the numbers came into this.

So, I think Dr. Froines' letter echoes what we just discussed here. I think it would be useful just to add this to the minutes.

DR. SIEBER: Jim, I'd like to read one sentence of his, which I particularly agree, and I think it's the undercurrent of what we just discussed about reevaluation.

He says in the second to the last paragraph, "The Panel should be open to a reevaluation of this compound's risk assessment values as more information becomes available," and the indications we're getting are that State agencies will be aggressive in trying to pursue that information. And to me, this is important. We need to have that kind of followup so that we don't wind up with a number -- it's the best number we can come up with today. But we don't want to be stuck with it.

If it turns out not to be the best number later --

CHAIRMAN PITTS: I think that's fairly correct, and I agree with it. I think the Panel does. I would make just one comment in this letter I think that's relevant, too. He says here -- let's see now. He says that he agrees -- he says, "The decision by OEHHA to use the value of 18.5 percent plus limit is highly consistent with

the scientific data, uncertainty," and so on. And then he says, "OEHHA has chosen to err on the side of health conservation, and that is entirely appropriate, given the state of the art available to it."

And then says, "The document presented to the Panel is clearly 'not seriously flawed" and it represents an extremely careful and sophisticated evaluation."

And he points out, "While some may disagree with the ultimate findings of the State, the review process, the evaluation, and all of the conclusions are highly defensible as a matter of science. And OEHHA needs to be applauded for its efforts as a balanced approach to the compound."

Now, are there other -- This is basically a public document, is it not? So, we will have copies, Bill, for the audience? There'll be copies availabile?

MS. SHIROMA: There are copies on the back table.

CHAIRMAN PITTS: All right. I agree with what you say. We might bring up the last paragraph in the context of a future -- why don't we at this time take a vote, an official vote. Let's look at the findings first. Let's go to the findings. And after we've discussed the findings, we'll come back with other comments.

MS. SHIROMA: George has some proposed language for Finding No. 3 to address Dr. Witschi's comment.

CHAIRMAN PITTS: Finding No. 3. Let's all look at these draft findings. Yes, George, go ahead.

DR. ALEXEEFF: I just wanted to add or suggest adding onto the findings -- on the third finding, where it mentions the range of unit risk, after it says, 2 to 72, at the end of that sentence, "remains unchanged," add a sentence saying, "The range incorporates lower metabolism rates and other model assumptions." Okay?

DR. WITSCHI: It incorporates higher metabolism rates, too?

DR. ALEXEEFF: There are some higher metabolism rates.

DR. WITSCHI: So then the range incorporates low and high.

DR. ALEXEEFF: Lower and higher?

DR. WITSCHI: Lower and higher.

DR. ALEXEEFF: Lower and higher metabolism rates. I think there's one metabolism rate that's 20 percent in one of the EPA estimates.

CHAIRMAN PITTS: Okay. Are there other comments from the Panel members with regard to the findings?

DR. BECKER: I make a motion that we accept those.

CHAIRMAN PITTS: Is there a second to that motion?

DR. FRIEDMAN: Second.

CHAIRMAN PITTS: Any further discussion? All those

in favor?

(Ayes.)

Opposed, no? It's accepted. And you might sit tight both of you for discussion. The findings are approved, with this addition, as presented.

Now, to get back to the point that was raised by both Dr. Becker and Dr. Froines, and, in fact, by Dr. Glantz -- is he in Canada today?

Yeah, he's in Canada. So there's a certain amount of -- I guess he Faxed. He couldn't mail us anything, at least with my understanding -- with my wife being a Canadian -- of the Canadian mail service.

Things are tough up there, too.

But we have also from Stan -- and he replied specifically to another letter from -- you mentioned -- Dr. Cammer to Mr. Strock. I received a copy of this letter with a cover message that says on it, "Please -- this is from Dr. Cammer -- "Please deliver the following pages to Lane Bailey from Paul Cammer, total pages 7."

It's got the message: "My secretary informs me you will foward this to James Pitts. Thank you for your assistance."

So, this letter came through -- although it's addressed to him, it was sent to me, and I gather it was sent to others in the ARB. So, my understanding, Bill --

Mr. Lockett, this can be treated as a public document, or discussion, or our response?

MR. LOCKETT: Yes.

CHAIRMAN PITTS: So, I think it's appropriate. We might want to respond to the -- some aspects in the letter. And maybe you would like to restate your comments initially, and then we can comment on --

DR. BECKER: The suggestion was that had been provided with a distorted, one-sided view of this science. And I don't think that that's the case, especially in light of the fact that I think we've been proactive to try to get to the bottom of it and understand it as thoroughly as possible.

And, in fact, I think we can turn it around and say that this is a good example that the process is working. We're certainly getting the information. We've opened the dialogue. And John's comments, I think, are very -- and perhaps I should read them.

CHAIRMAN PITTS: Why don't you read them, yes, and enter them in.

DR. BECKER: "Speaking as an individual, I strongly object to Mr. Cammer's conclusion that the SRP has been provided with a distorted, one-sided view of the data on perc. The SRP has had the opportunity to review the scientific evidence on perc presented by industry

representatives. Mr. Cammer's inflammatory letters to Secretary Strock and Dr. Lewis provide strong evidence why the Panel should consider any changes to its procedures very carefully in order to protect the quality of the scientific discussion. The issues concerning perchloroethylene have been carefully evaluated and I believe the Panel has a solid basis for a decision."

I agree completely with that. I was there at the meeting, and I think the process clearly is working. And I don't think that we want to change this process.

CHAIRMAN PITTS: I'd like comments from the Panel.

DR. FRIEDMAN: You know, any scientific arguments can always be clearly stated in concise writing. And I just don't see -- we're now addressing the thought that someone said we should open our meetings to the public for public discussion.

CHAIRMAN PITTS: Yes, this is the letter that has the major thrust that we should be opening it up to public discussion at the actual time we're evaluating the information.

DR. FRIEDMAN: Well, addressing that point, I really feel that any scientific arguments can be reduced to concise writing. And we can get these documents in writing, and we can evaluate them quietly or discuss. And

if we open this to public comments, we'll only be adding emotion to the consideration. And I just don't think that has any place here. And I would object to changing the format of our discussions in that manner.

DR. SIEBER: I would only add that the public workshop concept is working very well, in my opinion. And when I discuss our process, which incorporates workshops, with people outside the State, they're amazed that we go to that effort to get all the sides represented. So, I think it's a real strength, and I believe we used it to its fullest in this case, and have come up with a good conclusion because of it.

DR. DAVIS: I agree with the two previous speakers. My own feeling on this is that we don't need people with an angle and a point of view and a bottom line interjecting themselves in multitude within the context of what here has been very civil.

DR. WITSCHI: I have nothing to say.

DR. BECKER: I'd like to add that I think -- I don't know how anybody else does it, but Stan Glantz responded to something that I think is reasonable, and that is that many of us who get this large amount of paper will begin by looking at the comments in Part C first to get an idea about what the criticism is. And I think -- I can only speak for myself, but I found that some of the contents in

Part C have been some of the most valuable information. And I think that's excellent. I think I support that process. And I don't see how anything that could be put in Part C, how that would be improved with an oral presentation. I don't understand what the asset of that is. I don't see how that helps anything. So, I don't see any mandate to change the process at this time. And I don't think we should. And I would propose that we don't.

CHAIRMAN PITTS: Would it be appropriate -- actually, the last sentence of Dr. Glantz' letter, "Please enter this letter into the formal record should this matter come up at the meeting."

So, I would move that Stan's letter be entered into the record.

DR. BECKER: If my colleagues all agree, I think Stan's letter should be incorporated in our minutes.

It certainly echoes my feelings about it.

DR. FRIEDMAN: Not only that, but I would propose that we endorse it as the view of the Panel.

CHAIRMAN PITTS: Is that the motion?

DR. SIEBER: Well, would it also be possible or perhaps more desirable for us to draft a letter that incorporates all of our views and responses. Is that necessary in the case of this criticism?

CHAIRMAN PITTS: Sure. What we can do is to enter

his letter, and then the Panel could draft a letter which incorporates all the suggestions made. I think one of the points that should be kept in mind is, as far as -- from my experience on some of the exposure side of risk assessments and criteria documents, the EPA in the early days had a miserable time trying to ever come to some conclusion about some particular model or some particular type of measurements. And there was always new information that kept coming in. And it was unpublished data. And we've just got new data on this thing.

And these were criteria documents, sort of the basis for the control strategies. Finally, the basic idea came through that it had to be peer reviewed literature, peer reviewed literature in terms of final criteria documents. That shifted from 1968 through the years.

And I think that the Panel has been very clear, in that the OEHHA has indeed explored the existing peer reviewed literature; that's my impression. And it has, in fact, been more than happy to have received material which is accepted for in the peer reviewed literature.

And in another category, which has been wide open to us and has been transmitted to us,material that has been submitted to peer review literature. And, in fact, we have received and listened to developments from a variety of sources on material that's not even been submitted, but is

in the idea of reports. So, going along with what you say, Dr. Sieber, that OEHHA is involved and the Panel is interested in hearing this, and it has come to us through this range from something that's been there, into peer, all the way through to something that is, in fact, in the report stage.

Okay. I guess -- so, first of all, is there a motion first to incorporate Stan's letter in the official --

DR. BECKER: I think it does call for a formal response.

CHAIRMAN PITTS: Well, as Chair, I can just say to have that letter put in --

DR. FRIEDMAN: Why not both? Also Dr. Froines ' --

CHAIRMAN PITTS: Okay. Dr. Froines wasn't here, so I think it's appropriate to put his full comments in. All right. I'd entertain a motion to put the letters in.

DR. BECKER: So move.

DR. SIEBER: Second.

CHAIRMAN PITTS: All right. Both letters.

All in favor?

(Ayes.)

CHAIRMAN PITTS: Then do I hear a motion that the Panel then shall write a formal letter? This, I presume would go to Ms. Sharpless? That would be the appropriate person? There's Bill. That would be appropriate, would it

not?

MR. LOCKETT: Sure.

CHAIRMAN PITTS: And I think we should write to her in some reasonable period of time, so she'll have this available real soon. Is there a motion then to incorporate the comments from the Panel in a letter in regard to Mr. Cammer's letter?

DR. SIEBER: So move.

DR. BECKER: Second.

CHAIRMAN PITTS: All those in favor?

(Ayes.)

CHAIRMAN PITTS: Fine. Thank you very much.

I want to conclude by expressing my appreciation, particularly to George here, the staff --

DR. SIEBER: Jim, before we leave the perchloroethylene completely, we voted and approved the findings, the finding that we're going to communicate to Jananne Sharpless. However, there's a cover letter on there that I just wanted to return to, and I wonder if it would be possible if we reflect in that cover letter our interest, as the Scientific Review Panel, in seeing that new data be collected on exposure, metabolites, and things of this type.

CHAIRMAN PITTS: From whatever sources.

DR. SIEBER: That this committee give the State

agencies the kind of impetus they need to carry through on what I'm sure they would done anyway, but --

DR. ALEXEEFF: If I may suggest, there was also one of the comments that suggested that efforts be made to do epi studies as well of existing dry cleaners. You could add that as well. Of course, this is not a time to expend new resources, but it's something to think about and plan on how to do it.

CHAIRMAN PITTS: It would also be appropriate in the letter to Ms. Sharpless to basically state a position that I know that the Panel holds, and that's that we are also concerned about economic impacts upon the dry cleaners. And that's not just for perc. We're concerned about any definition of a particular toxic air contaminant, and a unit risk has -- we understand -- ramifications in terms of risk management. But we recognize that our function, as a scientific function of risk assessment, but we do understand there are these cost-effective problems that go along with health protective scientific evaluations. Would that be appropriate and useful?

Are there other comments? Okay. Fine. Now, I'm delighted to see -- I'd like to make a point about the next agenda item, which would be the discussion of the status of the Department of Pesticide Regulations, AB 1807, 3219, Tanner, air toxics identification and control program.

Dr. Jim Wells is here. I want to comment to Dr. Wells, he made the request that he go on at eleven o'clock, because he is a very busy man. Here it's eleven o'clock. We're one minute off. Contrary to certain unit risks, we are more precise at times.

But we welcome you here, and we appreciate your coming to the Panel to share your perspective from your new position, which is very important, from a variety aspects to society and science.

DR. WELLS: Well, thank you. I've got to tell you that I'm not one of those nice, well-meaning people from the Department that you talked about in your last meeting. I try to be nice. I usually try to be well-meaning, too, if it works out that way.

I am happy to be here. I've been hearing about this group for a long time, and haven't had the pleasure to appear before you.

After reading part of the transcript of the last meeting, I wasn't sure I wanted that pleasure, but I figured it was worth coming down anyway.

I've known Dr. Sieber and Dr. Becker for a long time, both through DEF, as it happens, which is interesting that we're finally getting around to doing something with DEF.

I don't know exactly what you want me to talk

about here, but I thought I would just basically sketch out the Cal-EPA and what our role is in it now and what's changed or what hasn't changed from the old days at CDA, and then run down a little bit about where we are in the process. It's a little difficult to talk about progress on 1807, since we have yet to list one pesticide since 1983, when the law was passed.

But, in fact, I do want to talk about the progress we're making.

First of all, we came in whole, in total, the whole Department, the whole Division of Pest Management came into Cal-EPA as a department.

And that means that we became the risk assessment capabilities and the risk assessment responsibilities that we had in Food & Agriculture. And if I really wanted to go back into history, I'd have to say that when 1807 was passed in '83, we really didn't have much in the way of risk assessment capabilities. That was prior to Senator Petris' Birth Defects Prevention Act and prior to our establishing of a toxicology branch, and hiring all the toxicologists. I think we had one or two toxicologists on the staff. Dr. Knakk was on the staff.

And so, we really didn't, in the first place, get staffed for doing risk assessment for 1807. We ended up being staffed for SB 950, the Birth Defects Prevention Act.

And because of that, we actually gained the expertise that we now rely upon to do the 1807 work.

When we came over into the new department, we joined several other agencies. We joined the Air Resources Board, as you know, the new office of Environmental Health Hazard Assessment, which came out of the Department of Health Services; the Integrated Waste Management Board; and the Department of Toxic Substances Control, from Health Services also.

So, that's the core of the new agency. And there are some discussions about the possibility of bringing in other environmental programs, such as Drinking Water from Health Services, and some other areas, as we go forward in trying to put together a comprehensive California EPA.

But, in fact, the way we came in as a complete department with our own risk assessment method, we stayed in control of 1807, just substituted the names. Department of Pesticide Regulation for the Department of Food & Agriculture, and Office of Environmental Health Hazard Assessment for the Department of Health Services.

Now, in the meantime, we had been attempting to get at least one chemical through the 1807 process. We have now asked ARB to monitor, I think, 12 chemicals. And we've gotten results for all 12 chemicals. And we've done a number of environmental fate assessments on that. And that

is the step that prepares them then for risk assessment in the medical toxicology branch.

Most notably, ethyl parathion, which you mentioned at your last meeting, has finally been completed. We tried one time a few years ago to list it as a toxic air contaminant, and basically didn't have the regulations in place that gave us the criteria to list it. And when we went to hearing, we were basically blown out of the water by the pesticide industry.

And so, we decided that in order to list a chemical, we had to have better criteria and regulation for what triggered a chemical being classed as a toxic air contaminant. So, we went back and put together a regulation that basically laid that out. It took some time to get that regulation through the process, and it's in place. Then we went back to ethyl parathion, and because it had been so long since we evaluated it, we had some new end points to look at. So, we put those into the process, relooked at ethyl parathion, and we've now pushed it forward to the point where we've announced it as a toxic air contaminant, and we're in the process of getting the regulation in place to designate it as a toxic air contaminant.

Right behind it is methyl parathion, which is going through the same re-review, now that we've changed the toxic end points. And that's close to finishing. So,

we'll have that finished within the next few months anyway.

And also sitting off to the side is paraquat, which we have pretty much completed risk assessment on. And when we get back to that after we finish methyl parathion, then we'll get paraquat listed.

And next in line behind that is gluthion, or azinphos methyl. But I think we're going to change that order. I think we're going to pull up DEF. And I think we're going to go ahead and complete, because DEF, in our Birth Defects Prevention Act risk assessment is close to finishing also. And that really brings up the substantive part of my discussion here.

And that is, if we don't quite operate -- I guess we don't regard 1807 in the way that the Air Board does, in that we look at multimedia effects of all chemicals. We basically look at the chemical outwards rather than look at a particular medium and say, what is the chemical affecting, or the chemical in this medium. We look at the chemical itself and say, what are all the sum total of exposures to this chemical.

And quite frankly, most often, the end points we're looking -- what we want to regulate on is not the presence of chemical in air, at least not in the ambient air. It's usually in the air of the worker that's mixing, loading, and applying the chemical, or it's in the air of the

adjacent community where it might drift, or it's actually because workers come in contact with it, or because of dietary exposure.

Those are most usually the end points that we're most concerned about. And so, consequently, some of the resources that we might spend on looking at toxic air contaminants, per se, is spent at looking at the exposure to the same chemical in a lot of different media.

And generally, that's where we find the critical problem. That's not to say that we don't review the information from the monitoring that's done in association with 1807. We do. We spend about a day doing a preliminary assessment of the monitoring data to see whether there's any particular urgency in dealing with that chemical.

So far, only one chemical has really popped out to be an urgent situation, and that was Telone. And we regulated Telone based on a set of statutes that don't have anything to do with 1807. And there's another point I'd like to make. Most commonly, because pesticides are already under a fairly comprehensive regulatory scheme, we are not generally depending on the 1807 law to give us the power we need to regulate.

If we find a problem with a pesticide today, such as we felt existed with Telone, such as exists with

methyl bromide right now in terms of the workplace, we have a number of other statutes and rules and regulations that we can employ to get control of that particular chemical to the extent to mitigate the risk.

And that's, in fact, what we do. So, basically, for us, 1807 is a systematic monitoring program, a systematic risk assessment program, but, quite frankly, we usually are getting to the same chemical sooner through one of our other responsibilities. And so, then, 1807 becomes part of the process.

And, in fact, at times, if we stopped to do -- to go through the 1807 process, we would slow down the risk assessment on the same chemical that you're concerned about.

And that's the case probably with azinphos methyl at this point. If we -- we're going to proceed with our risk assessment on azinphos methyl, and we will probably come up with some end points that need further mitigation, and we'll do that before or in spite of the exposure in air that we will eventually look at, because it's on the list.

And that's kind of a jumbled way to say it, but basically, the problem we've got here is priorities on our resources. We have to look at comparative risk of pesticides. And rarely is the air component of exposure

the important component, except in the case of immediate field effects. And in most cases, the authority that we need to control that situation is already in existence. There's maybe debate about how well we do it, but the authority is there.

CHAIRMAN PITTS: Open for discussion. Thank you. I think that's been very helpful. Jim, let's start out --

DR. SIEBER: Let me just make a comment. And it's kind of a question, or maybe asking for a rephrasing of your comment, Jim. It appears that most pesticides are fairly nonvolatile; so, in fact, the exposure by dermal or through oral ingestion and some other means is more important than the air inhalation component.

But could you give us a better sense on where pesticides lie? You mentioned methyl bromide and Telone as ones that could be of concern from an inhalation point of view, maybe guthion is something else. And among the universe of pesticides, given that there's more than 500 of them registered, can you tell us sort of how they lie now in terms of being potential air drift versus other media being more important?

DR. WELLS: Well, it's kind of difficult to put that all in context, but I think, generally, you're right. Generally, volatility is the key that we're looking at. And the presence in air, of course, is related to

volatility, but it's also related to the way pesticides are used. I mean, obviously, most pesticides go through the air in order to do what they're going to do. And so we expect to find them there.

You could take a strict interpretation of AB 1807, and we talked to Assemblywoman Tanner about this, and list everything, every pesticide that's ever applied as a toxic air contaminant, because pesticides are toxic. They wouldn't do what they do if they weren't.

And they generally are found in air; with very few exceptions, pesticides end up in the air somewhere. We're concerned about pesticides that have a high enough vapor pressure and are volatile enough that they are going to exist in what we would consider the ambient air, and that is away from the field at some distance where the general population is affected. Admittedly, that's kind of our own definition, but that's -- when we're looking at comparative risk, that's what we're looking at.

Generally, when we're regulating pesticide even in air, we're regulating in the workers' breathing space. And that's what we're most concerned about.

Methyl bromide's a good case in point. We just recently took some steps to adopt emergency regulations for methyl bromide in home fumigation. We started there because that's the most uncontrolled population exposure. You can't

really predict what's going to happen in a home and who's going to get exposed. So, when we determined that the numbers we had on methyl bromide, that the end points for toxicity were far lower than we originally determined them to be, the first step we took was to modify the way methyl bromide's used in the home.

The second step is to look at how it's used in field fumigations, again, primarily with the worker in mind, but also with the offsite movement of the material to adjacent housing, et cetera.

And thirdly, commodity fumigation, and we took that third, because it's probably the most controlled situation with the least exposure. And we know that basically from experience, not from data.

So, that's kind of the way we look at it. I don't know if that answers your question. But when we look at all the potential risks of a chemical, and most of the chemicals that are listed on 1807 turn out to be the same ones that we're looking at in our Birth Defects Prevention Act, or the same ones that we're looking at when we do acute data -- where there's an acute problem. It's all the same list. There are probably 25 or 50 of the five or six hundred you talk about that we're really concerned about, and that we're going to look at in all media. Paraquat is a good example. Paraquat is not a terribly volatile

chemical. It's a very toxic chemical, but it all depends on the route of exposure. And so, it's true, paraquat is sitting there. It's applied through the air a lot. It causes a lot of nontarget quite toxic effects on plants. But in terms of general population exposure, it's not that high on the list, or at least exposure to the general population is not that high on the list or a reason to control paraquat.

So, it's on our list of 1807 chemicals. It's coming up. It will be evaluated, and you will get to review our report on it. But we're not hell bent for leather to get that particular chemical regulated under 1807. We have lots of other ways to regulate it.

DR. SIEBER: I think Jim's comments are really important to us, because we need to look at our list in terms of our own prioritization and the order in which things are considered, And maybe the choices that were made several years ago that led to the existing list need to be reexamined, because he's already mentioned methyl bromide and Telone, things that weren't, I don't believe, were even on the list to begin with, or maybe they were pretty far down in the priority list.

Maybe they should be brought up. Maybe there's others -- ethylene oxide, or whatever -- that may fall in the same volatility class. So, I think this is an important

comment we need to consider as a Panel.

CHAIRMAN PITTS: Dr. Witschi, comments?

Dr. Davis?

DR. DAVIS: We're all citizens, and I think that that's the frame of reference that I come to on this Panel. And I don't really have any interest, financial or otherwise, in the chemical industry, including what they put in my car for fuel. I hope that Chevron makes a lot of money, because it'll help Northern California's economy. But I don't want to do anything at this seat in order to advance their fortunes. And I was concerned, like I think several of us were concerned the first time we went through with the Agriculture bunch, that it was a marching chowder society between growers and the regulators, where the regulators were boosters of California agriculture. And they couldn't be boosters and at the same time sort of put the brakes on the efficiency and effectiveness of California agriculture.

So, I looked at their paradigm as entirely different. It's pretty obvious that he knows what goes on in agriculture and the chemical use, and what the situations are in a way that it's not clear that I knew about this list of chemicals we've been going over and over and over.

I know my closet, when I come home from the dry cleaners smells like that perc stuff for almost a month.

But that's as close as I can get it at home.

DR. WELLS: We do know a great deal about how chemicals are used, not just in agriculture, but in general. And I don't think that we could regulate them otherwise, especially when you get into the process of comparative risk. The more you know about the exposure situation, the better you can regulate. And I think that, despite the fact that we did have a dual role in Food & Agriculture to promote and protect agriculture as well as the public health, you'd be hard-pressed to find a farmer in this State that didn't think that the regulation we brought to bear on pesticide areas didn't cost them money, considerable amount of money in the last 15 or 20 years to put them at a considerable disadvantage with other growers that they compete with in other states.

So, yeah, we did have a problem there in perception. I don't think no matter what we did we ever would have been -- gotten away from that if we had stayed in Agriculture.

We could have done the most Draconian regulation in the world, and we would have been accused of doing it because that's the way the farmers somehow wanted it, even though nobody could quite understand why it was that they wanted to be regulated that way.

And as such, I think, you know, being in Cal-EPA

is going to help that quite a bit. Over the years, I'm sure that personnel will change and that we'll probably become less familiar with agriculture. And that's probably unfortunate. We're going to become less familiar with all the areas that we regulate, but I think it's inevitable.

What we need to try to do -- and most panels and most groups tell us this all the time -- is understand the industry you're regulating, because then you don't make as many mistakes. And as much as we know about agriculture, we've made a lot of mistakes in trying to regulate it.

DR. SIEBER: Jim, I had one other question here that seems -- it seems to me that a lot of our reasons for looking at pesticides like DEF and paraquat come from the possibility that there's an ultrasensitive population out there that either becomes nauseated or perhaps has respiratory symptoms when these chemicals are being used.

Now, that could be real. And I guess the question is, what are we doing to find out whether those are real things or whether they're perhaps imaginary?

MR. WELLS: What we're doing to find out basically is monitoring the exposures, looking at the levels, and looking at the data and calling-in data, obviously having studies done that we don't have on file now

to try to determine what is causing that problem. DEF is a good example. As you know, the years I've spent down in Fresno looking at DEF, regardless of whether the active ingredient in DEF was causing illnesses -- something was causing illnesses. And, yes, we went out there time and time again and interviewed people who were sick. You can say, well, it's just the odor. But what is the odor? It's butamercaptan,which carries a certain toxicity. So, we need to deal with whatever is causing the problem.

The difficult thing to deal with, of course, is the ultrasensitive people or chemically sensitive for allergic reaction type things that only affects a small percentage of the population. It's very difficult to deal with and to separate out from other toxic effects.

And I don't know that we will ever get to the point where we're not going to put anything in the air or there's not going to be anything in the environment that an ultrasensitive person will react to.

Our goal is to look at what is the real toxicity, what is the end point we need to regulate to, what is the significant effect level, and how do we mitigate the use down to that level. If we can't mitigate the use of that level, then we get rid of the material.

In terms of fumigants, a good example of that is ethylene dibromide. We're still dealing with ethyl bromide.

It's still out there. People are still being exposed to it. We're attempting to mitigate those exposures down below a level of significant risk. The determination was made with ethylene dibromide several years ago that there was no way to mitigate it down below the level of significant risk.

So, we just got rid of it. There are a number of other chemicals that have fallen into that, generally not because of ambient exposures, but because of some other exposure where we just could not mitigate the risk to the end point we wanted to.

So, that's not a good answer. There always are going to be the chemical sensitives, but to separate that out from the toxicity and the general population that we need to deal with -- again, most of the time, it's the worker population we get to first. And if we protect them, the rest of us are home free.

DR. SIEBER: Are there epidemiological studies that you are aware of or perhaps sponsoring that deal with this problem of sensitive or ultrasensitive populations, in the farming communities, let's say?

DR. WELLS: Well, there are a couple things underway with the Ag Safety Center. And I wouldn't say we're sponsoring -- we sit on the Advisory Board at the Ag Safety Center and comment on those studies. We don't

currently, that I know of, we don't fund any studies like that. We would depend on probably Lynn Goldman's group to do epi studies over at the Department of Health Services, or perhaps the Office of Environmental Health Hazard Assessment. But we don't have those kinds of programs going on.

DR. SIEBER: Jim just gave me an opening to give a pitch to the University of California's Agricultural Health and Safety Center at U.C. Davis, and I believe that's the organization that you're mentioning --

DR. WELLS: Yes.

DR. SIEBER: -- that's in the process of gathering some of this data. So, I've handed out a brochure that describes the center for those of you who are not familiar with it. I think most of you are.

DR. WELLS: We have in the past anyway -- not done any epi studies, but when Dr. Lotti was out from Italy, we worked on a study to try to determine -- to try to look at biological indicators of exposure to workers. So, we've done a lot of that kind of work. It's not epi studies, but we have been involved in exposure studies ever since Keith Maddy got there in 1969.

DR. BECKER: I think one of the things that's been troubling to us before was the question about the registration process, how the air exposures to the general

population is taken into account. There's a big difference between looking at an adult pesticide applicator and what his cholinesterase is by comparison to a child one month whose cholinesterase hasn't been fully developed yet. And we tried to find out information about that, and it wasn't all that clear what the information was.

So, I'd be interested to know what currently goes on in the registration process when the general population is taken into account, the specific population -- the children is one thing about sensitive populations. There's another thing about the normal population as a whole, what impact would say cholinesterase inhibitors have on the population. I think we would like to know how that's addressed.

DR. WELLS: Generally, when we do risk assessments, we take advantage of every route of exposure that we have data on, which includes air exposure. And that's one of the ways that really 1807 is a help to us, because it is a regular monitoring program. And even if we haven't completed a compound through that program, we do have the data that we can plug into the risk assessment, the general risk assessment.

There's a certain amount of comparative risk analysis done at the front end. And from a day or two's review, our toxicologist can often determine what the most

sensitive end point is.

Then we also look at what the most sensitive population is. We do that in dietary exposure, and we do it in ambient air monitoring. For example, when we did find parathion in the air down in the Central Valley in the fog, then we followed up and we looked at those levels, and we looked at sensitive populations, including children, in determining whether or not we thought there was an unacceptable exposure. We came out with a determination that there was no significant risk even to the most sensitive population.

So, the problem often is we don't have the best information we need to make that determination, and that's what the process is all about. But, once we have it, we look at the most sensitive population, and it isn't always children. Dietary exposure, depending on what particular item in the diet is, it could be, you know, teenagers. They eat more hamburgers than anybody else does.

So, you have to look at the most sensitive population that will do that. If we fail anywhere there, it's because we don't have adequate data to determine what the effects are on the sensitive population. And so, obviously, we extrapolate from the ambient data, and we build in the margins of safety and margins of uncertainty.

DR. BECKER: You get to be proactive about that.

That was an example of the cholinesterase data that was critical to deciding about population, and that information wasn't available. I was pretty surprised and most of the members of the Panel were pretty surprised when we went over that, something as fundamental as a cholinesterase in a fully developed, six months of age, how much more at risk, and where does that fit into the population as a whole?

CHAIRMAN PITTS: Are those data available now? I'm just curious. If they aren't, why don't we get them? Why doesn't somebody get them?

I know it's money, but this is a high priority it would seem to me.

DR. BECKER: I talked to Dick Jackson about it, and it's just a question about more proactivity. How do you prioritize getting that information?

I guess I'm speaking for Stan Glantz, because he had a question about why the process was so slow. And I guess part of it was that we were just surprised -- I was surprised about something that was fundamental as that. That information was not known.

Like, as an example, when the question of methyl bromide occurred, well, the question came up, well, has anybody ever looked to see whether or not methyl bromide was in the water beds or not. And I couldn't get

that information. That's fundamental. If you're going to do a house fumigation, there's going to be water beds in there.

DR. WELLS: I'm not exactly sure. We found out during the spill in the Sacramento River that there's a lot of data there that hasn't been collected for a particular purpose, but suits that purpose. For example, what would happen if methamsodium is spilled in the river? Nobody ever developed data on dumping a tank car in a river. But we were able to determine what the breakdown ratio in the water was.

Unfortunately, we didn't have good enough studies to know what the dilution factor of it was. And that confused us for a while.

You can't anticipate every piece of data that you might want. On the other hand, we are sensitive -- especially to acute exposures to children. And we are counting to some extent on what the NAS report says and what some of the failures are in that process so that we can correct some of those failures.

We're subject to, obviously, the data that's there. And our being able to anticipate the data needed depends a lot on what the exposures are. So, it's kind of a holistic process. It wouldn't make any sense for us to go spend a lot of money and a lot of time developing

a lot of information on a chemical to which a sensitive population isn't exposed.

CHAIRMAN PITTS: We need a lot more information. But we are going to be exposing young children. We know this. And what mechanism exists on the part of the Panel and you, in your division, to encourage someone else to put money in the Act for research, to focus on something which is as relevant.

I know you've never -- none of us here has ever been involved with this thing called malathion, right? But I understand that works in terms of the cholinesterase situation. And we're all aware of what went on. And I was called on a number of occasions about this. I was asked some questions, and I raised the question about malathion about children, the effect on young children. And I said, "I don't know what happens."

But I do know there are concerns about ethyl parathion, and there is a target, very young people that have a problem. And that's something that certainly should be investigated.

And the second thing that came up, as a chemist now -- and again, it was fascinating to me -- was the incredible potency of the certain impurities in the methyl parathion. I mean, people that got knocked off by methyl parathion, apparently a very large number of those

were killed by the impurities, relatively small amounts of impurities.

Now, I did not see when they sprayed methyl parathion over a very large area of Southern California, I kept trying to find out in here, were they spraying technical pure, 100 percent malathion upon which very often toxicity -- okay? It's like saying getting data on toxicity of ozone when you put ozone in pure air and expose it, is it the same as it is when you get smog and have ozone; it's a very different milieu.

So, I was very concerned about that. Maybe, Jim, you probably know what it was, but I think the public ought to know. If these exposure tests are going to be run, toxicities are evaluated, they should be done in terms of what technical grade of malathion is, in fact, being sprayed.

The third thing is, it's really important -- it fascinates me. I'm interested in chemical transformations. Simple stuff, you know. Like smog, ozone.

What changes in regulations have been made or proposed on the basis of shipping methamsodium? But it applies to other toxins that, in themselves, are basically nontoxic, but when they hit the environment, become very highly toxic. Has anything been done for that chemical? Are there rules now that weren't there when the disaster

occurred?

Are there new rules that are now in place saying, this is not, per se, a toxic; but exposed to environmental conditions of the following type, which now have happened?

DR. WELLS: I'm not familiar with this, because it's out of my area, the transportation thing. But SB 48 contains some requirements on transportation. There's a limitation, because of interstate transportation on what the State can do in that regard. Because it's federally preempted, so it's not going to deal with interstate commerce.

And so, things like the kind of cars that the material has to be transported in, the kind of manifest it has to carry, and things like that. We tend to have some problems with federal regulations, but the Public Utilities Commission also has authority there. And I know there have been some changes. The PUC requires certain documentation, that information be available as to what kind of materials are moving through a county available to the county, and that kind of thing.

If that had been a tank car full of milk falling into the river at the concentration that would have resulted -- we would have had dead fish. You know, it's interesting that it was a pesticide. Because the milk would have taken the oxygen out of the water. We

would have had fish die of oxygen starvation basically.

So, you know, you're not going to require data on what happens if your tank car falls in the river. But I think it's reasonable to require that information be -- at least accompany that shipment so that, when it does fall in the river, people know what the hell's in there.

And that is being addressed.

CHAIRMAN PITTS: Okay. What about this question, a real serious question of spraying pesticides on that are not -- when you have data that come in on toxicity that are done versus what is really out there in the real world and what is really introduced into the atmosphere and the environment?

DR. WELLS: Depending on what the material is and what the toxicity of the metabolites or the impurity, we do look at that. We look at butyl --

CHAIRMAN PITTS: (Interjecting) You mentioned that. That's interesting.

DR. WELLS: We looked at that as far as what people were being primarily exposed, at least at some distance from the application. And parathion, malathion, aldocarb, we're looking at the oxones and the oxenes as well as the parent compound when we're making our judgments on risk. As a matter of fact, all of the malathion work -- we monitor, we sample all the applications.

And we monitor when the material is delivered. We take a sample when the material is mixed; we take another sample out of the boom. And all of that is run through analysis to see what material is actually being put out.

So, to the extent that we know that information, or that we know that that's a concern, we're able to evaluate it. And tolerances -- dietary exposures. So, it's not the dark hole that some people think it is. Admittedly, we can always use more data. But, I'd like to follow up a little bit on that, too. We talked -- some of the things you're talking about, about needing some data on cholinesterase inhibition, et cetera, is an area that's been probably neglected over the years. And that's the acute data program. Senator Petris came in in 1984 with the SB 950, Birth Defects Prevention Program, which basically caused us to call in a lot of chronic data for chronic effects.

But when we went back and looked at the acute database, we found that the acute database itself is pretty lacking. And in one way, you could say we're not as worried about the acute database, because if there were acute problems, you'd see them. But on the other hand, when we're constantly registering chemicals that don't have an adequate acute database, we're concerned about that.

So, we actually sponsored and got incorporated

into the Bronson bill, AB 2161, of Acute Data Call-In procedure, so that we can upgrade that database.

Unfortunately, there's no money for it. And if we were really going to sit down and do a comparative risk analysis, and if we just took all of our statutory authorities -- 1807 included -- and laid them on the table and said, what's the most serious problem? What's the most critical problem; what is the end point we really need to be looking at and to protect the population in general, we might throw out some of the programs that are mandated right now that we're obligated to conduct, and instead use the money from those programs to do something else that doesn't have a mandate.

So, you're always in this situation where you've got a statutory mandate that sounded good at the time. You may have another whole area that you really feel you need to look at, but you've got to take care of your statutory obligations first, and you've got shrinking budgets.

So, you know, comparative risk is a very important thing. Cal-EPA is going through what will probably be a two-year comparative risk assessment project to try to look at where we ought to put our money. And that's going to be very important in the future.

DR. SIEBER: Another comment about pesticides. I think the real problem, the real dark hole is one of

accountability when the chemicals are used. And most of them are applied by air in this State as opposed to other states where a lot of them are applied more to the target. If they're applied by air, and you go out later and look for them, you can maybe account for one percent or half a percent of what was released. And we presume a lot of that winds up in the air, but we really don't know. Some of that breaks down. So, the overall environmental big picture is very poorly understood.

When you have that much unaccounted for, people are always going to ask questions. Where are these things going? That's the kind of information, it seems to me, needs to be developed. And I know it's tremendously expensive having you do it, but do you have any comment about that, Jim?

DR. WELLS: Well, the 1807 program, you know we have monitored 12 or 13 different chemicals in the air. A lot of the time we don't find anything. And we're using all of the information that we have, all the intelligence we have about what's the most critical time and most critical place to monitor to target the request to the ARB. And still, most of the time, they're not going to find anything.

I think you're right. I think you need to constantly monitor, and that is an expensive process, and we

are going through it with 1807 to some extent. Again, we're not finding the number of things you might imagine we might find in the air. And it's problematic, because sometimes when we don't find a chemical in the air, it causes us to work harder at the assessment end, because we have a chemical -- if we have the number, we can do a risk assessment based on the number; if we don't, we have to figure out what's a conservative number.

We haven't really slowed down. Even though we're not fully processing all these chemicals through the 1807 program, we haven't slowed down on monitoring. We're still pumping them out.

And again, I can't emphasize enough, that when something happens that really catches our attention, and we look at that and say that this is an unacceptable level, we don't wait for 1807 to kick in. We already have authority. If we find something that gives us concern, we move on it.

DR. SIEBER: At least as much and perhaps more so than other State agencies, this Department and its predecessor is subject to all of the spills and the Mediterranean fruit fly crises. I think that's what diverts them from gathering a lot of this interesting information. They're constantly being pulled by one crisis after another. You have a couple of people being

killed in Redwood City because of methyl bromide fumigation, and pretty soon their whole program is over looking at house fumigation. So, it's very hard to have a sustaining program when you have a group that is so pulled by crisis.

DR. WELLS: I've got to say this. We were looking at methyl bromide before people got killed. It was actually Senator Petris' bill, and the call-in data that triggered the methyl bromide examination. But, you're right. Generally it is. We tend to be headline driven. You know, the amount of time you put into a spill -- a better example, watermelon. Aldocarb came in 1985. It was a tremendous amount of effort just to make sure that every watermelon that we shipped after June 19th of that year didn't contain aldocarb.

DR. SIEBER: I just have one other comment. Since a lot of the pesticides are applied through the air by aerial applicators, that -- some people believe that's a source of some of our problems with drift and material entering the air. A better way would be to get the chemical on the target more efficiently. Is the Department also sponsoring those types of management programs where they're looking at better ways of using chemicals? It's not the chemical; it's how you use it, right?

So, what's going on in that area?

DR. WELLS: Well -- I'm trying to think of the name of that system is, the magnetic system.

DR. SIEBER: Electrostatic.

DR. WELLS: Electrostatic spraying. We did a lot of work on that and determined that it wasn't quite the panacea that it looked at. We've done a lot of work with the engineers over at U.C. Davis in trying to develop ways to modify aircraft, basically both in the procedure that they use and in the equipment that they use to prevent drift. We did that with cotton defoliants. By using bigger nozzles and bigger drops, you get less volatility and get less dispersion of the material. It tends to drop straight down. We've required thickening agents to be included with certain kinds of materials in the tank mix so that it helps keep the droplet sizes bigger. There are certain size droplets that we know will drift more readily than another size droplet. And there are ways that you can modify application equipment to achieve a higher proportion of those size droplets in the spray.

So, we've done all those things where we felt we really had a problem. It has been more in terms of preventing drift, trying to keep that material on this field instead of the neighbor's yard next door, and we've been active in that area. Yeah, that's all part of the

process.

I would posture that that will be in the future going to be a bigger role for the Department of Food & Agriculture now that we're out of it. I think, in the future, somewhere down the road, pesticide regulation is going to become just what it says, pesticide regulation. And a lot of the things that we used to do to encourage new technology is going to be taken over by the Department of Food & Agriculture if there's ever a budget that anybody can operate under again in the future, which may be some time.

And when we find something that works as a mitigation measure, and mitigation is absolutely necessary, as in the cotton defoliants, then we can implement that by regulation regardless of what the pesticide label says.

CHAIRMAN PITTS: Other questions? Well, if there are no other questions or comments, I want to thank you on my behalf personally and on behalf of the Panel, for your presentation and your presence here. And we appreciate that very much.

So, we would be more than happy to interact with you. I remember back -- and I think Bill Lockett was there -- on one of the presentations some years ago, when methyl parathion was made so that it never leaves the field. That's in the record. And things have changed. And

we're glad to see the emphasis on drift and interactions with our two groups, which can be very helpful all the way around.

DR. WELLS: One thing we need to think about, and I'm sure it's been said here before by people from Food & Agriculture who appeared before you, we look at 1807 for chemicals that are basically unregulated, bringing them under -- into toxic air contaminant status, gives people the ability to regulate them when they may not have regulated them before.

We do have the ability to regulate pesticides. And another thing I want to stop off into just briefly, and I'm really getting out of my league here, but -- because I'm not a scientist -- but there are -- I think we'd like to sit down with a group of you and talk about the way you want to see the data that we present. Because we've got the ongoing risk assessment process, and we create that data in a certain format as exposure data as part of the whole process -- whether it's dietary, air, water -- we create a certain format. To redo that into the format that you guys want to see it in is expensive and time-consuming.

Maybe we can sit down and talk about the format it's in, and maybe accommodate that a little differently.

CHAIRMAN PITTS: It's a good idea. Sounds great.

We can notice it and put it on the agenda.

Well, on that note, we'll again express our appreciation, and look forward to interacting with you.

And we are now going to Item 3, and we can have a very brief discussion, perhaps 10 or 15 minutes, on Item 3, the OEHHA's cancer risk assessment guidelines. And, George, perhaps you and Dr. Zeise can come up and do that now.

(Thereupon, there was a brief recess taken, while the reporter replenished her paper.)

CHAIRMAN PITTS: Okay. We may begin again.

And we'll have sort of an initial discussion, an overview of the status of the Department of -- sorry -- the OEHHA's cancer risk assessment guidelines. And what I'd like to do is to turn the chair over to Gary Friedman, Dr. Friedman, who's the leadperson from our Panel on this particular subject. And, Gary, the floor is yours.

DR. FRIEDMAN: Well, we had a nice phone conversation the other day just introducing me to your effort in this. And so, we believe the whole Panel would like to hear about that, and particularly the question that I raised with you as to why you're doing this at this time.

DR. ALEXEEFF: Dr. Lauren Zeise's group is actually

the lead within our department and within the agency on revising the cancer guidelines. So, she'll present our current efforts. And I'm going to now turn into a Ph.D. projectionist.

DR. ZEISE: Thanks, George. The guidelines that we're talking about are the 1985 guidelines that were signed by Governor Deukmejian and developed by the Department of Health Services. And these address the hazard identification and dose response evaluations for carcinogenicity.

Now, one of the reasons why we're doing this update is because, in the 1985 guidelines, we promised that we would reevaluate the guidelines periodically. There's been a lot of recent information and some new methodologies that have been proposed and, in fact, used in some of the risk assessments that the Panel has seen.

The guidelines, to a certain extent, address these methodologies, but not in detail. So, it's time now to reevaluate and extend and provide -- so that other State staff can use these methodologies. So, that's one of the primary reasons why we're doing it.

One example is, there isn't one sentence in the guidelines that say, pharmacokinetic data shall be used. Well, the question is, how shall they be used? What kind of models, what criteria do we use. Another issue that comes

up frequently is uncertainty analysis. So, we hope to give that adequate coverage in the update.

Now, the staff within Cal-EPA, and that includes OEHHA, the Department of Toxic Substances Control, the Department of Pesticides, or sorry, DPR -- Dr. Wells' group -- and staff within these groups have been meeting to discuss the issues that come up and should be addressed in this update. And several key areas have been identified.

Now, we've outlined these issues and our basic approach to them in the overview -- I don't know if you all have a copy of the overview, but I have some extra copies here if you'd like to refer to it. The first issue that we're looking at is carcinogen identification. Our current guidelines take a simple approach. Either something is identified as a carcinogenic hazard or not. Shall we be more detailed in this? What about using other information besides animal bioassay information?

Use of genotoxicity data. Can this information be used to guide us in our selection of dose response relationships? How can we take into account genotoxicity information when we go about an attempt to identify agents as possibly being carcinogenic with just limited animal bioassay or even no bioassay information?

Can we use genotoxicity information for that

purpose?

In terms of dose response modeling, lots of information has recently come out about various mechanisms of action for compounds. Take, for example, the dioxins and the dibenzofurans? How can we incorporate that mechanistic data into dose response modeling? Should we? What criteria do we use to include this information?

In terms of standard procedures for cancer potency evaluation -- let's say we don't have any mechanistic information or any adequate information on other mechanisms of action besides genotoxicity. Again, we are faced with doing a standard dose response evaluation.

Should we change any of our standard procedures? What do we do when there's very little survival of the animals that are being treated? Are there procedures that we should apply to this kind of circumstance?

With respect to interspecies extrapolation, there's been a lot of discussion about interspecies extrapolation factors for default risk assessment or standard risk assessment. Typically, we scale on the basis of amount per surface area in going from small animals to large animals. There have been recent arguments that instead of doing this, we should scale according to the three-quarters power, that this more approximates what might be happening metabolically. Should we change in that direction?

There has been some very interesting recent information developed by Dr. Dedrick down at the National Cancer Institute who looked at cancer chemotherapeutic agents that were tested in laboratory animals and then given, as part of cancer chemotherapeutic treatment, to humans. And what he has found is that cumulative milligram per kilogram dose seems to be a better scale. So, in fact, the information that he is developing is actually going in the opposite direction of the three-quarter scaling power. Basically, he's indicating we're not being conservative enough. So, we're trying to look at that issue.

With respect to using epidemiology data, a number of questions arise. And one of them is in terms of absolute versus relative risk models for describing the dose response relationship. There are other issues as well that come up. Pharmacokinetic data has been discussed here over perchloroethylene, methylene chloride.

In terms of uncertainty analysis, in applying these very complicated models to data, are there additional procedures that we should be using to take into account the uncertainties in the parameters? How about just in cases where we have very limited information, should we go further in trying to characterize the degree of uncertainty that we -- that is involved in developing these dose response

relationships?

And then, finally, with respect to human heterogeneity -- just earlier today, we heard a lot of discussion about differences between sensitive children and adults. And now, for carcinogenesis, there are several fairly good examples of cases where the population differs considerably in their sensitivity. There are different levels of isozymes and different subpopulations. Should we more formally take these issues into account in our evaluations?

So, those are the key areas that we're focusing on. And we hope that, if we're missing any, you'll tell us about it. And in the overview that we sent out, we indicated where we might be going, and we'd like as much input as possibly early on in the process, so that we can adjust and take into account the issues that are missing or areas where we might be a little off the mark in our approach.

We're very interested in any comments from as many of you as possible.

DR. SIEBER: One thing that occurs to me -- I know it's buried under some of those others, like uncertainty, but the problem of mixtures. And I think we're going to face that square away with environmental tobacco smoke. I think that's going to turn out to be the usual way in which

people are exposed. It's not just a single chemical, certainly in ambient levels.

So, it seems like that might be one you might want to consider adding to your list.

DR. ZEISE: Thank you.

DR. BECKER: And I have this -- we spend all our time talking about carcinogens, at least my time on this thing. And I think we're going to see cardiovascular, neurobehavioral, so I don't think I'd limit your concerns about risk assessments just to carcinogenicity. I would prefer that we don't just focus on that, and we give some thought to other end points and how you would treat them differently. In other words, the uncertainty -- cancer is a dichotomous area. Don't just limit yourself. That would be my suggestion.

DR. FRIEDMAN: Is that, though, within the scope of this work? Because I notice it's guidelines for chemical carcinogen risk assessments. Would that be beyond that you had planned to do?

DR. ZEISE: Well, we actually do have another set of guidelines in development for reproductive toxicants. So, we are addressing those end points as part of that guideline and --

DR. BECKER: They have to be consistent, though, and you have to explain why they aren't consistent. And

I think reproductive, neurobehavioral, cardiovascular are going to be the next generation of --

DR. ALEXEEFF: We had a presentation from someone from Lauren's group a year ago on the status of reproductive guidelines. And just now, we just had a meeting a couple weeks ago that Lauren's group put together to start looking at the other end points, exactly what you're talking about, the other noncancer end points. And that is in much more of a formative stage. And particularly, we are focusing on EPA's -- US EPA's recent focusing on what's called a benchmark dose calculation for noncancer things.

So, we're working with both -- other Cal-EPA agencies in trying to look at the noncancer end points. But that's not going to be covered in these particular guidelines. But, please keep pushing us, and we'll keep trying to develop something. But that definitely is the next area of focus.

CHAIRMAN PITTS: When you do this -- I'm wondering at the next meeting, when you go into detail about this, will you also present to us the status of where you are on neurotoxicity. As an old chemist, I think of lead as being both a possible carcinogen, but its neurotoxicity. And you get accurate numbers there. I'd like to see -- maybe you could show us how, for something

that has two possible problems -- formaldehyde interests me as having a number of effects that aren't simply carcinogenic.

That's something you might want to think about and then fit it into a pattern, as Dr. Becker was suggesting. On ETS, it's certainly going to be that way. So, I would hope that you could maybe even put some emphasis on what he's suggesting, that we have a consistent, coherent view -- and I might add that's important also not just from the toxicity, but from the exposure side.

DR. ZEISE: Well, one thing that might be helpful is we could give you a report on the outcome of this workshop where we looked at methodologies to analyze noncancer data, and to give you an idea of the kind of issues that came up and where we're thinking about going with these.

CHAIRMAN PITTS: And also include a page or two about what you think of it. In other words, that helps me. I'm not too competent to judge this, but -- but if you would say, here's the report, and here's how we see this fitting into this plan. That would be a basis then for our moving ahead.

DR. ZEISE: Okay.

DR. ALEXEEFF: I think that's possible. And also, I think that probably the next set of guidelines that we'll

be presenting will probably be on acute toxicity assessment. We have some draft ones internally, so at some point, we'll be bringing them to this Panel.

DR. WITSCHI: I would like to make a general observation about the use of mechanistic data, which I think you're all in favor of. But it occurs to me that what I've seen whenever or invariably, the mechanistic -- when the mechanistic data are being used, the result is the carcinogen becomes less potent. All the results of mechanistic considerations so far go in one direction. And they tend to make data which are derived from a bioassay as overly conservative.

There might be some reasons for this. Maybe that's the truth. Maybe also you can design those kind of experiments to go in the direction you want them. Maybe it's who does those experiments.

So, I have very, very mixed feelings about -- I would urge some caution in embracing cell proliferation, or metabolism, or all PDKs, or all those kinds of things. Because so far, if you look it up -- I may be wrong, but I still have to see an experiment which shows that a substance was more potent than it actually was from the bioassay.

DR. ZEISE: One of the interesting things that's coming out of the detailed work on dioxin is, for that

particular class of compounds, it's actually cutting both ways. And the level of information that's coming out of those experiments -- so far at least with the work that's been done at the NEIHS -- seems to indicate consistently with something more conservative or less conservative. So, when the work is very, very careful, it's unclear where we'll end up.

This is another reason why we want to be very careful also then to look at the human heterogeneity issue, because as we become more mechanistic in our approach, we must realize that people have different sensitivities. And if we do become less conservative, then we need to take into account the more sensitive members. So, this is another reason why we're focusing on that.

I have some more transparencies. I'm wondering if maybe this is the time to go into more detail here, or --

DR. BECKER: I think we can wait for the full report and read it.

CHAIRMAN PITTS: Let me ask you one question. I think we discussed this before. In this whole thing, how are you addressing or will you address this huge controversy of the animal bioassays? That may be a part of this, but I would sure like to hear or have something in my hands that says in relatively straightforward terms

that even I can understand -- again, you've mentioned this, but why this approach is being used, and looks at the approach that we're talking about -- cell proliferation and all that -- and says at this stage of the game, this is whatever your view is.

I'd just like to have that for my own -- to answer questions from -- that I get from a variety of sources. And I'm not qualified really to answer them.

Would that be possible?

DR. ZEISE: As part of looking at the issue of using additional data, we will be looking at the cell proliferation issue.

CHAIRMAN PITTS: Good.

DR. ZEISE: And then in terms of hazard identification or determining whether or not certain data -- types of data should be used to identify carcinogenic hazards, we'll be looking at the issue of relevance of certain kinds of results to identify something for humans as a possible hazard.

So, we hope to get adequate coverage of those areas.

CHAIRMAN PITTS: Are there other questions? Well, if there are not, then, we express our appreciation to you again. And we'll be seeing you.

We have the question of another meeting date. Do

you want to address that at this stage of the game? I'll go to Mr. Lockett here.

MR. LOCKETT: I think what we need is to recognize that you need to fill out the calendars that we gave you for the next months.

CHAIRMAN PITTS: We dropped June 18th.

MR. LOCKETT: That's why we need to find a new date for the next meeting. The next compound, there's a workshop in the summer, so it would come to you probably this fall.

DR. BECKER: So we look for our next meeting in the fall?

MR. LOCKETT: That would be my guess.

CHAIRMAN PITTS: All right. If there's no other business, why, we'll adjourn the meeting. Thank you very much.

(Thereupon, the meeting was adjourned at 12:17 p.m.)

--o0o--

CERTIFICATE OF SHORTHAND REPORTER

I, Nadine J. Parks, a shorthand reporter of the State of California, do hereby certify that I am a disinterested person herein; that the foregoing meeting was reported in shorthand writing by me, and thereafter transcribed into typewriting.

I further certify that I am not of counsel or attorney for any of the parties to said meeting, nor am I interested in the outcome of said meeting.

IN WITNESS WHEREOF, I have hereunto set my hand this 31st day of May, 1992.

Nadine J. Parks
Shorthand Reporter